

Motif 2

Motif 3

Motif 4

Rv2837c_Mt	YVWCHVHPDADTIGAGLALALVLDGCG	[35]	VDLVVTMDIPSVDRLGAGL	[6]	RELLVIDHEASND	[10]
s111253_Ssp	DLILCHQTAEDFDVLGAAGVGLAKLHKGSR	[34]	IRSLXIVENQOGDRGKIA	[8]	RQVAYDHHLNSP	[11]
MGPA_Mg	IVIPHHVRPDPGCLGAQGCLPHLKANF	[32]	EALAIWVDANYKNRIELRE	[7]	KAVLRIDHFPNED	[11]
YTQI_Bs	LILHHRVHPDPDAYGSQCGHTEI1RETY	[30]	GALVYVDTANQERIDDR	[4]	AKLMKIDHFPNED	[11]
AF2029_Af	LGIPTHDNPPDSMSSAYALREIAKQFD	[37]	YDFAIAIVPSSSGPGVUNNSIP	[3]	DISIVDHHHPAEK	[10]
MJ0977_Mj	NKILIVTHILADGLTSRAIIQKLAERLN	[23]	YDLIIIPADLGSGQLMKIE	[11]	DKIILDHQPEE	[18]
MJ1198_Mj	RPIIIRHHADDGYCGGALEKAIIPLII	[46]	LPLIVTLDNGSTDDEIDPAI	[7]	IEVIVDHHFPGE	[85]
HP1042_Hp	MQVHLHSIDLDGACOLVSKQFFPKNQ	[27]	EFLIIVSDLNUNLNEAVL	[13]	IQIQLDDHISGK	[19]
RecJ_H1	QKIVIVGDFDADGATTSTALSVTALRQLG	[31]	VOLLMTVDNGVSSFGVAF	[5]	IRVLVTDHALPPE	[33]
RecJ_Hp	TEIIVVGDYDADGVISSAIMAKFESLN	[27]	APLITIVDNGINAFAEARF	[5]	YTLITDHHCLHH	[27]
RecJ_Ssp	EKVTIINGFDADGITSTAVMEGLCQFF	[32]	TKLIVTDGTGSTNLDEIVY	[5]	MDVIVDHTLTPD	[27]
YBQ_Bs	ILIFGHONPDTDTICSAIAYADIMKNG	[36]	VNGVILVLDUNEROQSIIKDI	[3]	QVLEYDHERIAN	[12]
ICRA_Sg	ILVFGHQNPDSPAIGGSSYAFAYLAREAY	[38]	AEQVILVDPHNEFQOQSYADI	[3]	EYGVWHDHRYAN	[12]
Y608_Mj	RYVUGHKNPDTDSIASAIVLAYFLDCYP	[31]	GKEIIILVCHSEKSQSFFDL	[3]	KLIAIDHFKVGL	[19]
AF0756_Af	VYVUGHKNPDTDSVCASIAFAYWINKWK	[46]	GKKVALVDHSEKAAQYDGI	[3]	EVVAIDHFKIGD	[12]
U60409_Lm	TVVQGNEGGMDSIVGCCIYIAMLFDKQP	[44]	QIAHNLDIAALNASVWLY	[14]	RWGVWHDHFDDEQ	[11]
PPX1_SC	TICVGNEASADYDSIASAATYSSCYIYN	[62]	ELNSYLVDDNDTPKONLKNY	[2]	NVVG1DHDHFDLQ	[14]
PRUNE_Dm	HLVGMGNESOOLDSAVSAVTLAFTVYAQRH	[48]	DVNVLVWHDHVSPLAPNT	[1]	NVTEIILDHRLPED	[18]
h-PRUNE_1	HWVLGNEAQDLDSTVSVALALAFTYAKTT	[52]	QLTLLVWHDHILSKSDTAL	[2]	AVAEVLDHRIEPIE	[12]

Specific motifs

Specific motifs	Grs
TWNLAASVGCGGCHRLAAGTTTGS	1648883
DTDLTQLEPYYGGCGHAAQAAVNLRDV	1653244
GIVNRDIAIKYGGGGHNNASGAIITNK	1045875
GPIVNGLARKYNGGGHPLASGASIYSW	2293259
BVLRRAFGDGSACGGHAAHAGAQIPLG	2648507
DTDLTQLEPYYGGCGHAAQAAVNLRDV	2129221
DTDLTQLEPYYGGCGHAAQAAVNLRDV	2129221

1

Familj 2

PRUNE_DM
b-nomine_1_Hs [31] DISALTEVLRKDNKVAQID [31] ERQAVNQAIKKA-TLPVAK [31] VIGGENTOVSRSK-KLPVLOE [31] 11245938

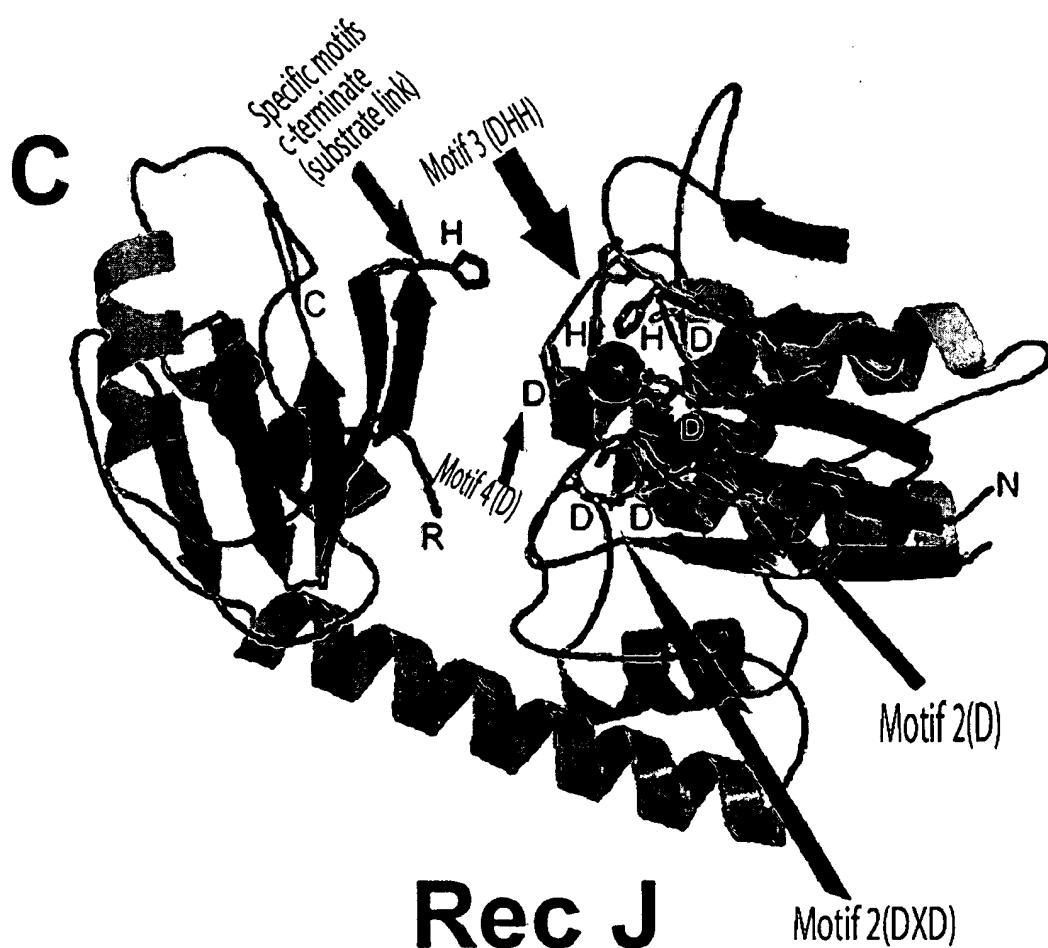
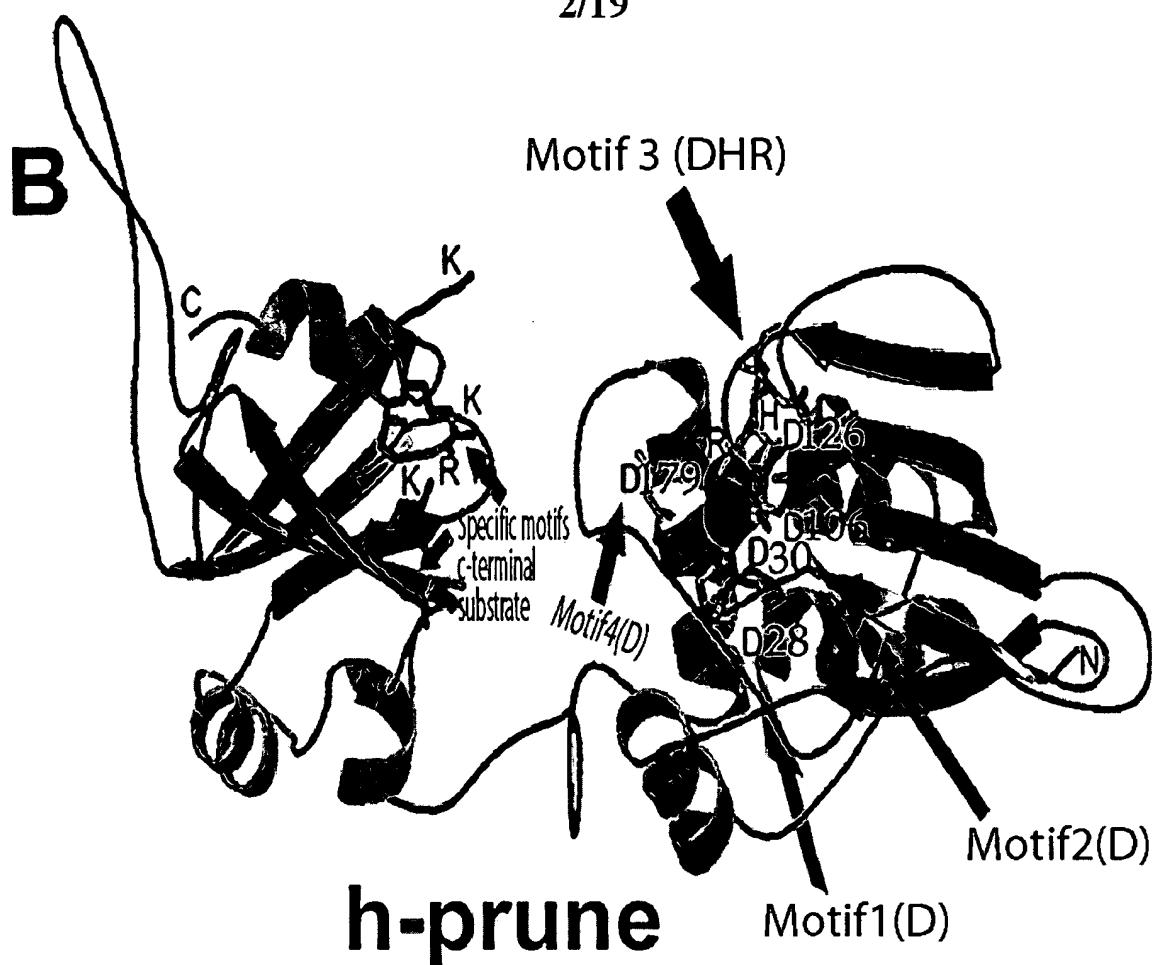
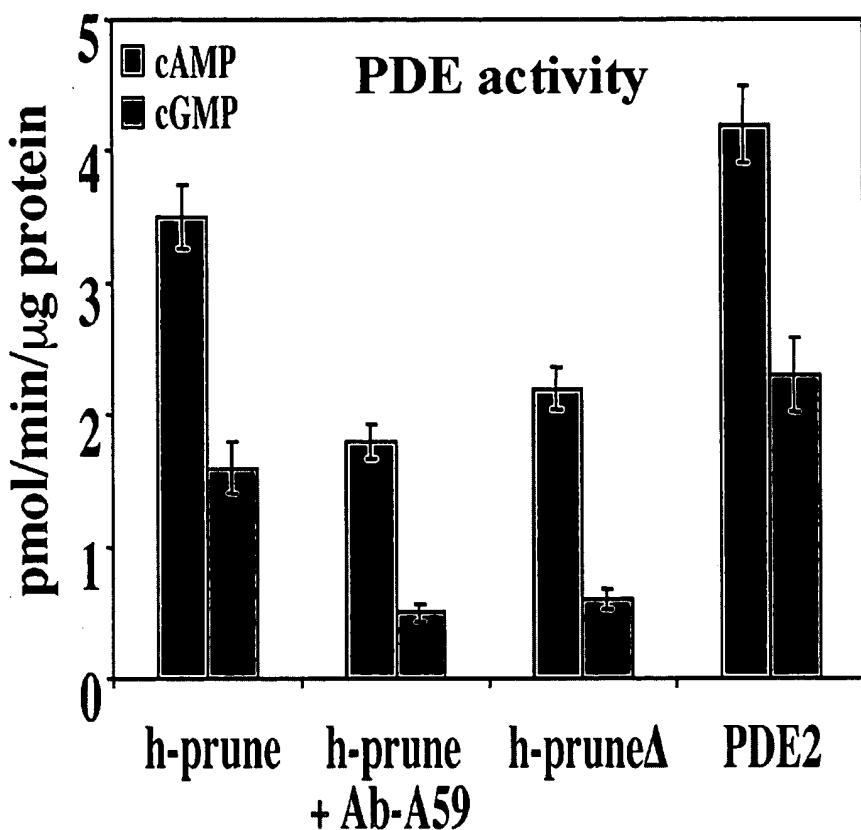
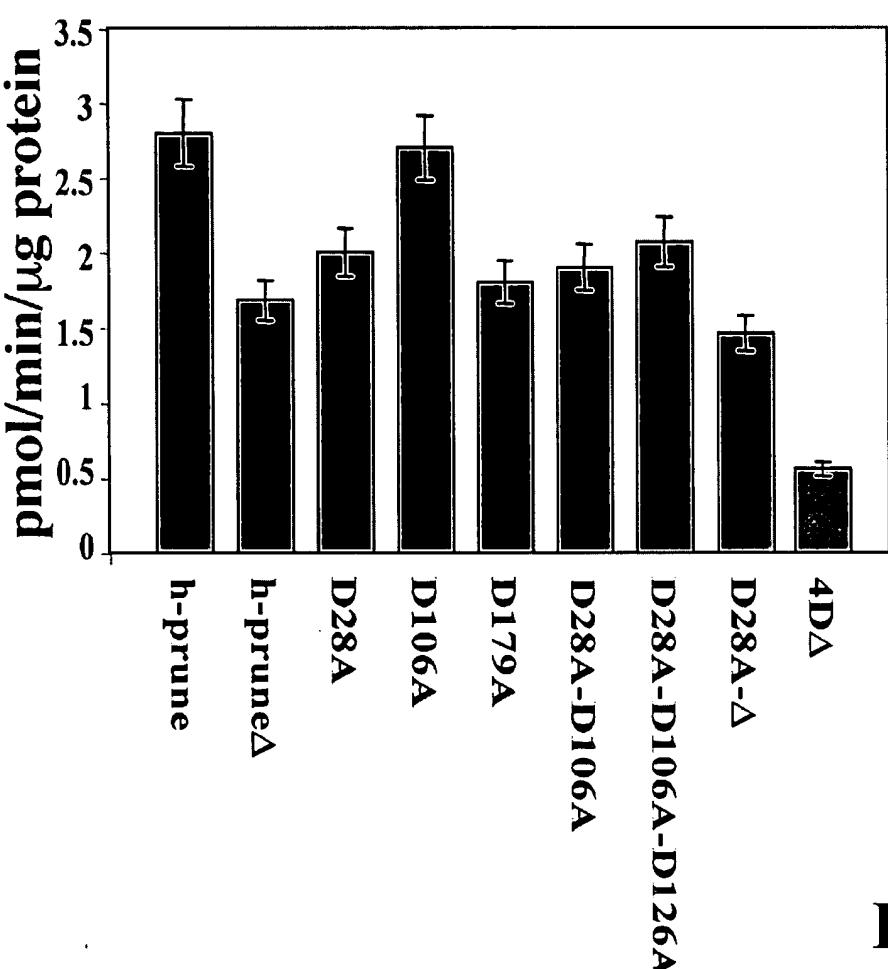


Fig. 1

A**B****Fig. 2**

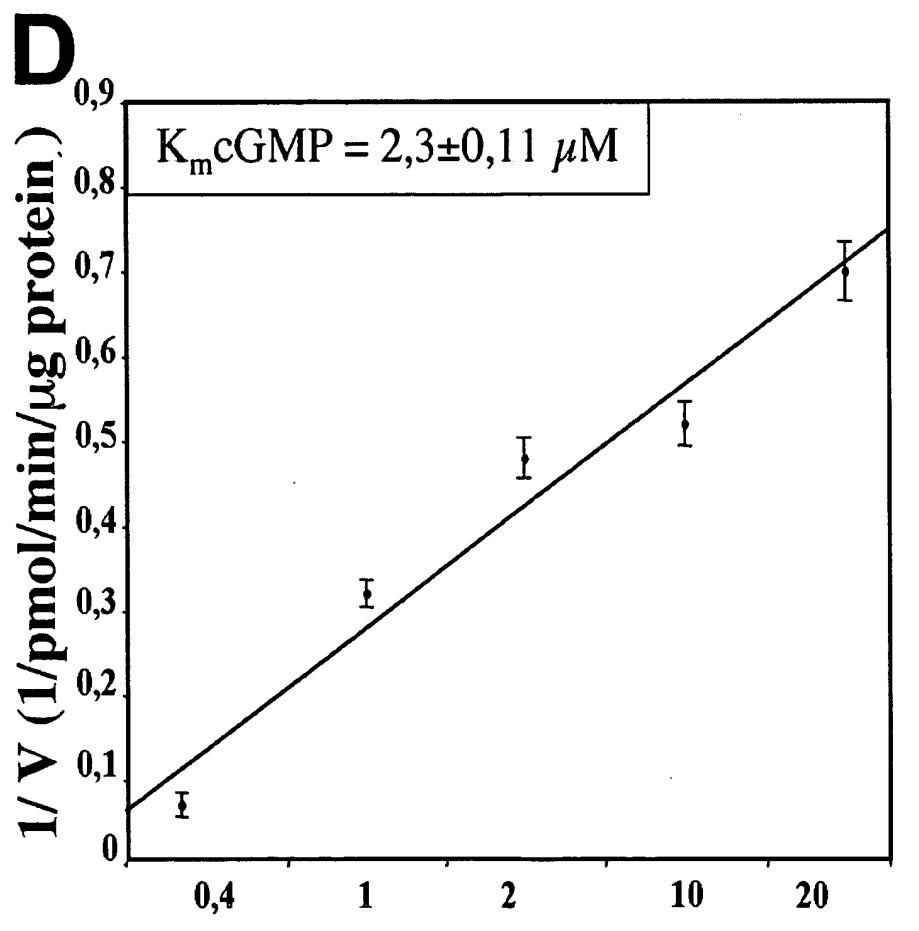
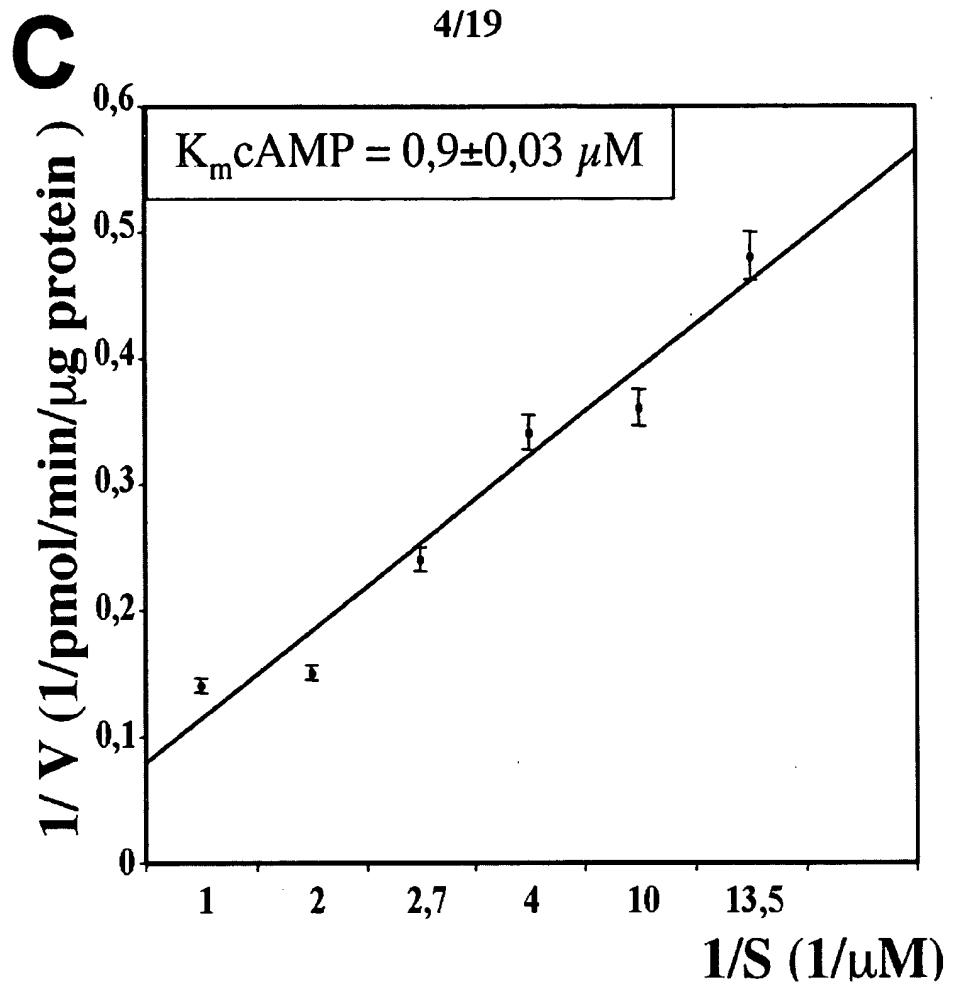
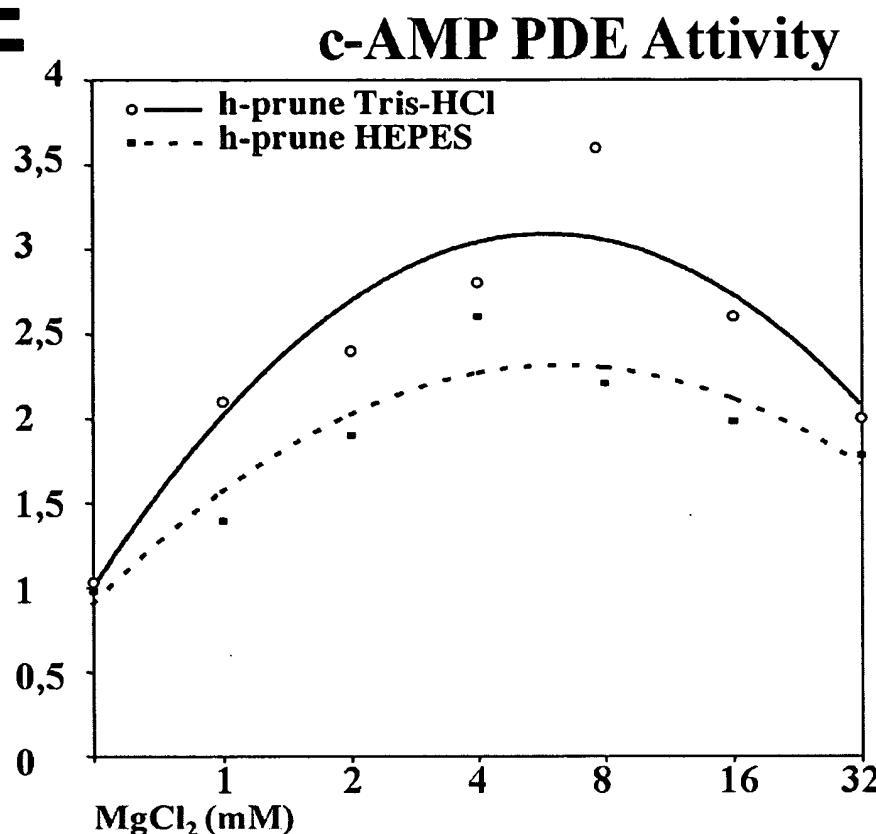
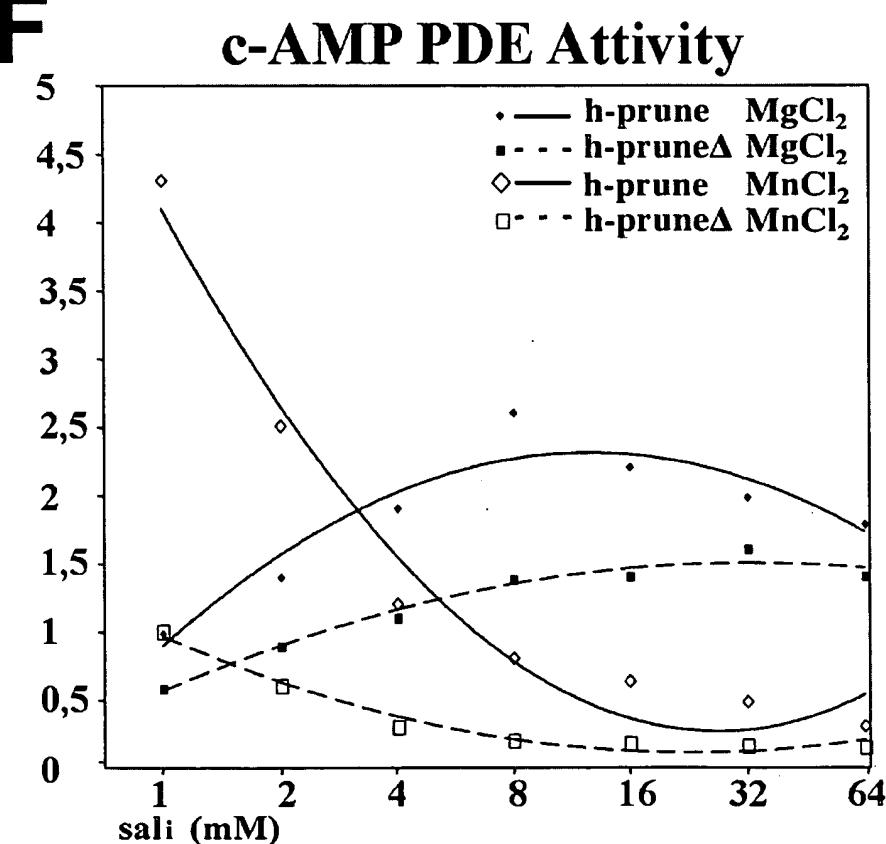


Fig. 2

$1/S \text{ (1/}\mu\text{M)}$

E**F****Fig. 2**

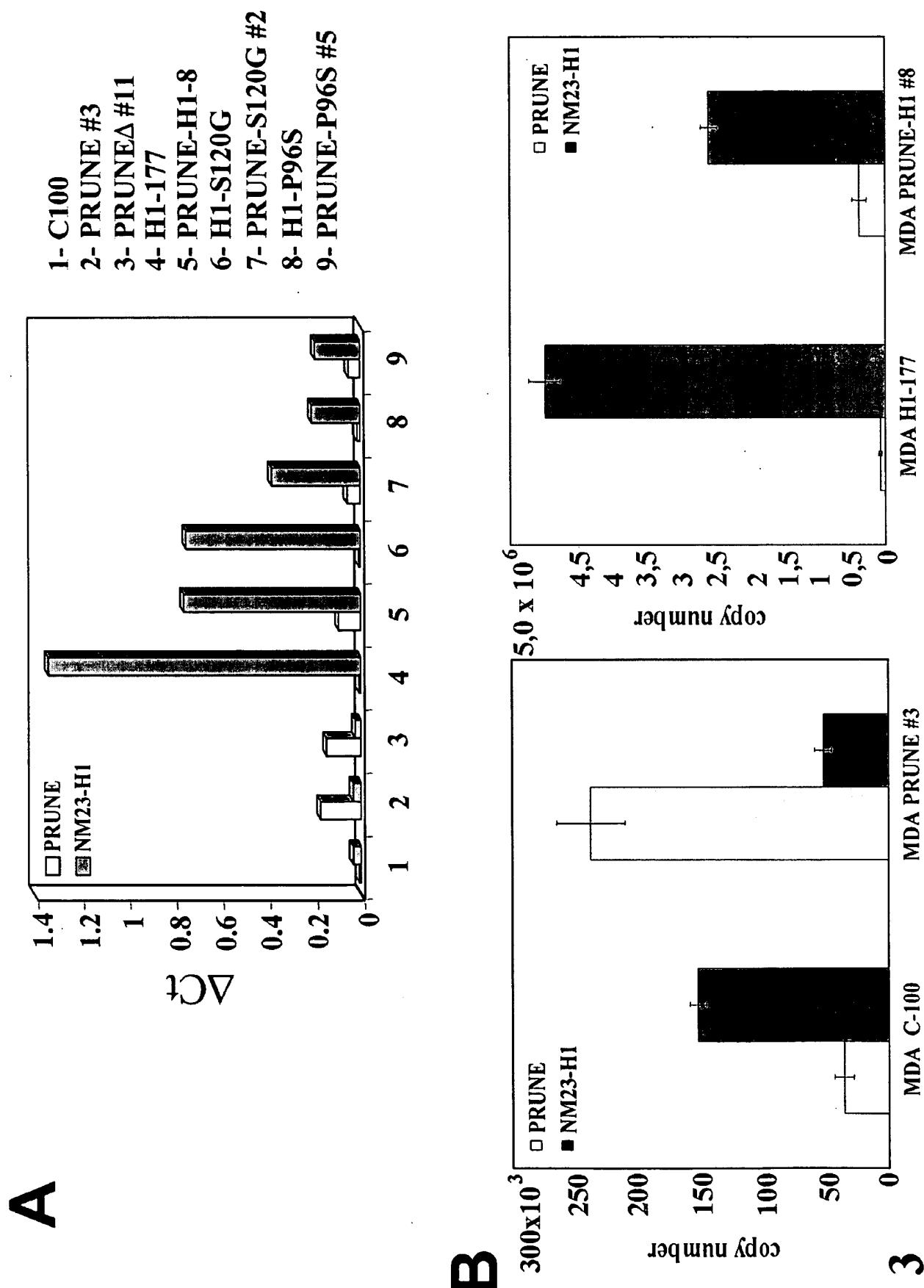
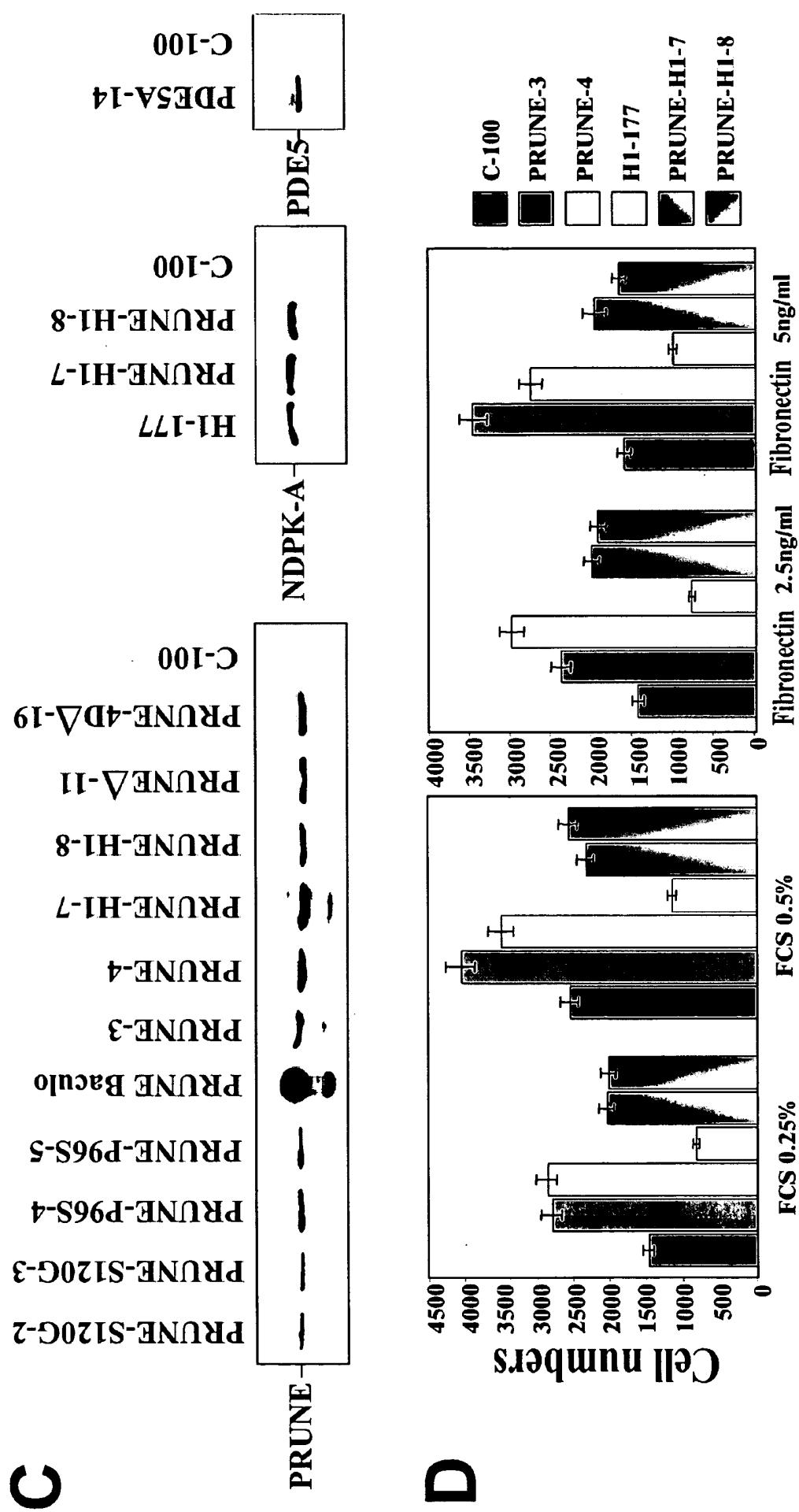


Fig. 3

**Fig. 3**

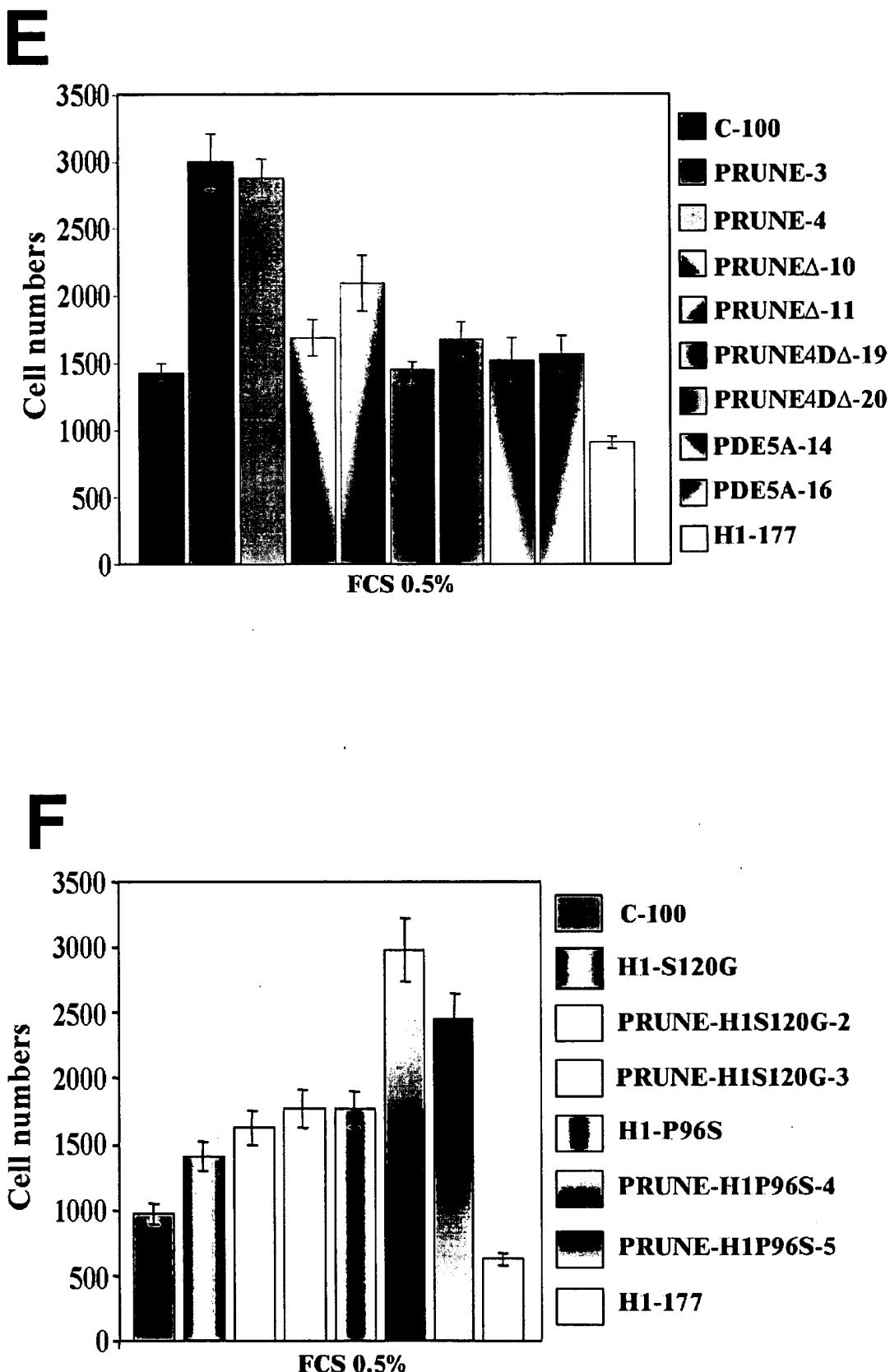
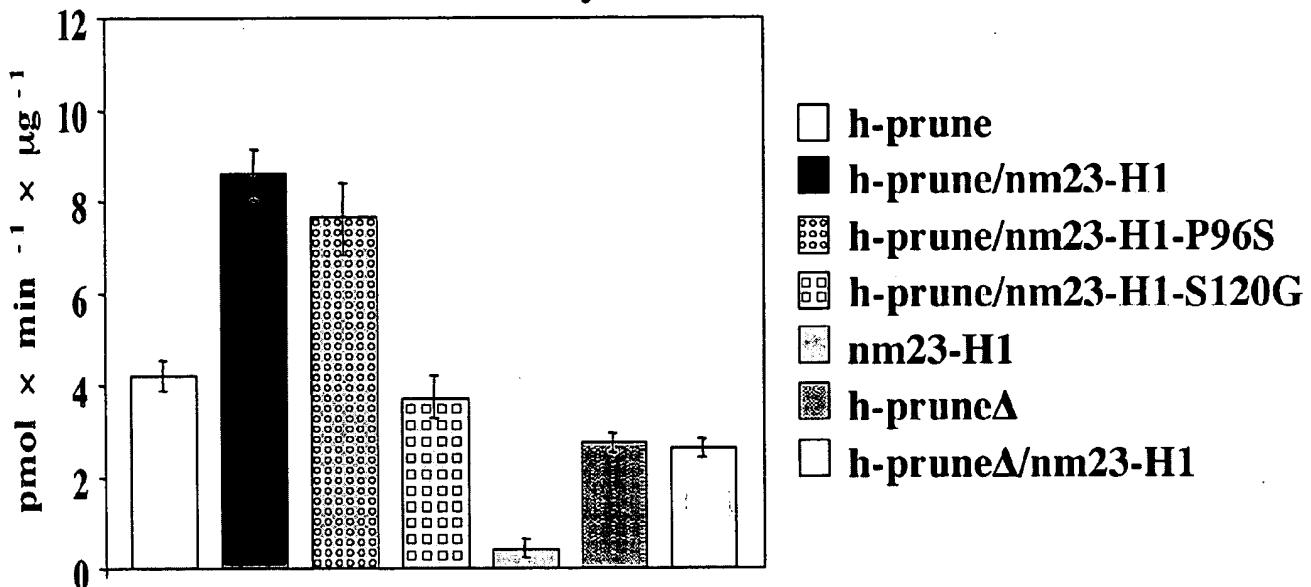


Fig. 3

A

c-AMP PDE activity



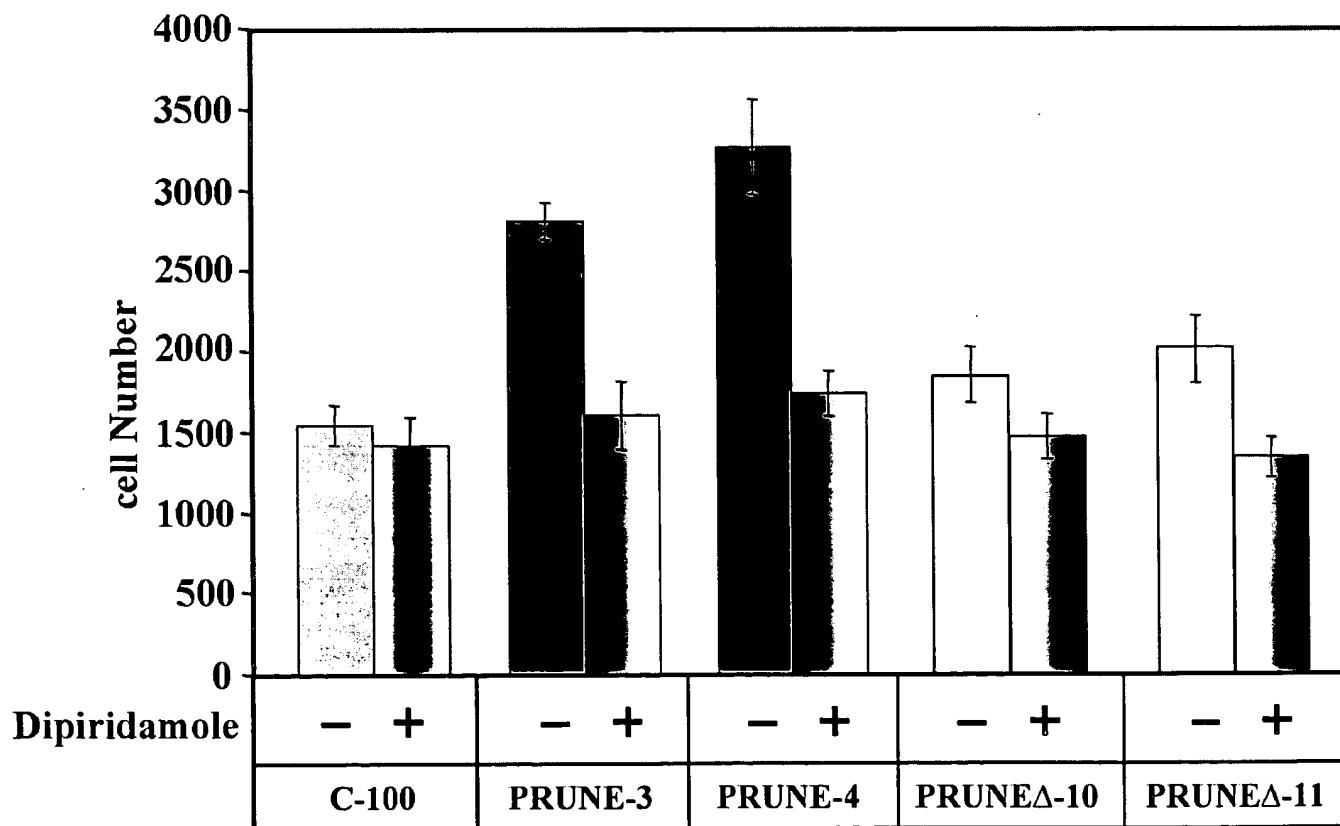
B

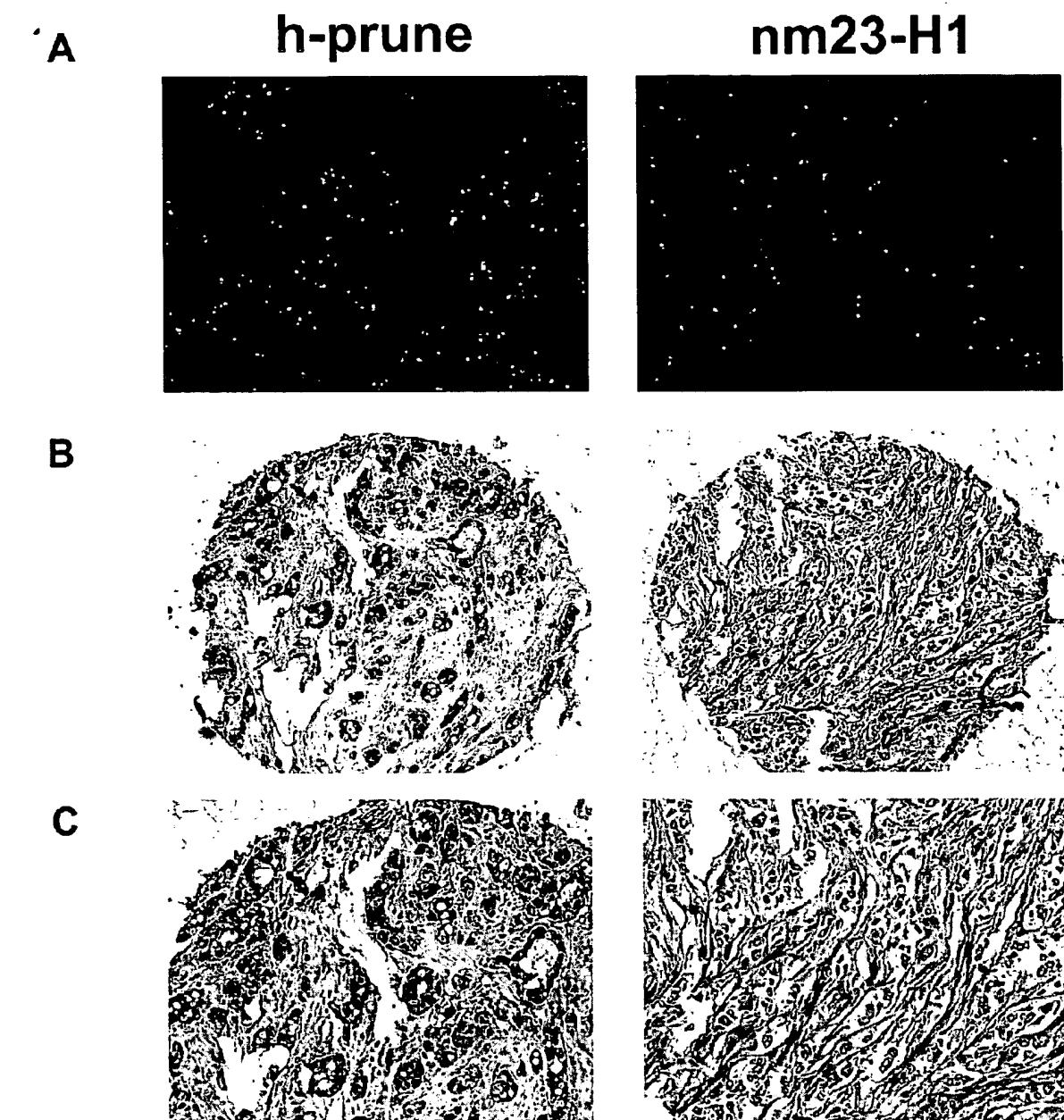
clone name	PDE h-prune Activity (pmol x min ⁻¹ x μ g ⁻¹)	Mobility cell number
MDA C-100	3.8±0.7	1548±84
MDA H1-177	2.2±0.4	928±73
MDA PRUNE #3	35±5.3	2812±294
MDA PRUNE #4	28.7±2.5	3272±271
MDA PRUNEΔ #10	16.8±1.2	1682±64
MDA PRUNEΔ #11	14.6±0.9	2087±97
MDA PRUNE-H1 #7	18.8±2.6	2048±93
MDA PRUNE-H1 #8	22±4.2	2006±87
MDA H1S120G	2.4±0.8	1328±54
MDA PRUNE-H1S120G #2	4.4±1.6	1624±89
MDA PRUNE-H1S120G #3	5.3±1.4	1767±108
MDA H1P96S	3.0±0.3	1742±38
MDA PRUNE-H1P96S #4	19.2±0.3	2982±184
MDA PRUNE-H1P96S #5	11.6±0.4	2448±143

Fig. 4

A

Inibitor	Selective for a PDE type	$IC_{50}\mu M$	h-prune $IC_{50}\mu M$
Cilostamide	PDE3	0.05	>100
Dipiridamole	PDE5/6/9/10/11	0.9/0.38/4.5/1.1/0.37	0.78±0.05
IBMX	not selective	2-59	40.2±0.8
Milrinone	PDE3	1.3	>100
Rolipram	PDE4	2.0	>100
Vinpocetine	PDE1C	8.1	22.3±1.1
Zaprinast	PDE1/5/6	6.9/0.76/0.15	>100
Sulindac	cGMP PDEs	—	>100

B**Fig. 5**

**D**

Immunohistochemical (IHC)	IHC Grade	Fish analysis			
		PAC h-prune (1q21.3)		PAC nm23-H1 (17q21)	
		Disomy	Trisomy or more	Disomy	Trisomy or more
h-prune	+++/++	7 (12%)	22 (37%)		
	+/0	30 (51%)			
nm23-h1	+++/++			1 (2%)	
	+/0			54 (98%)	
analyzed cases TNM1		59		55	

Fig. 6

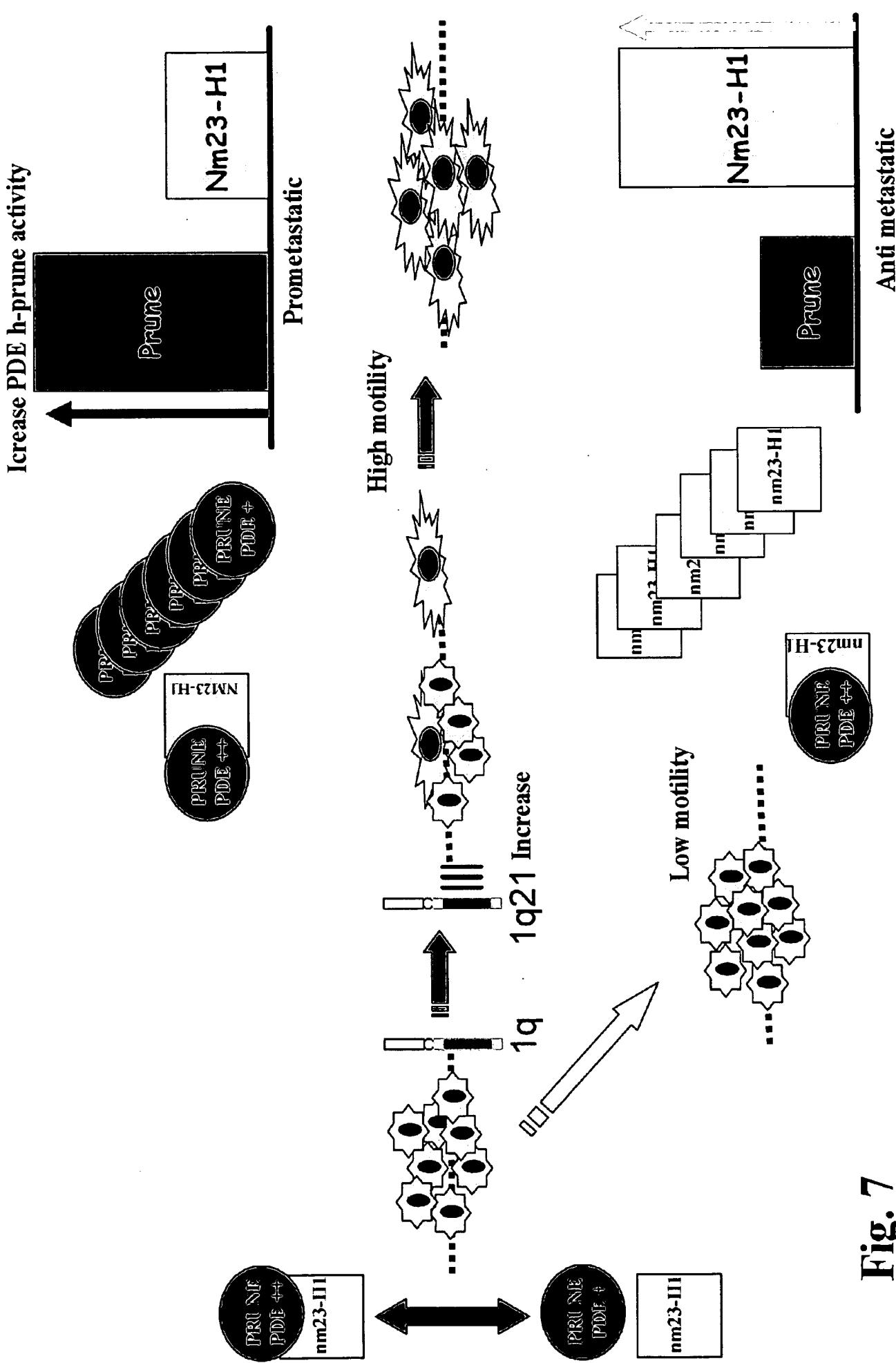
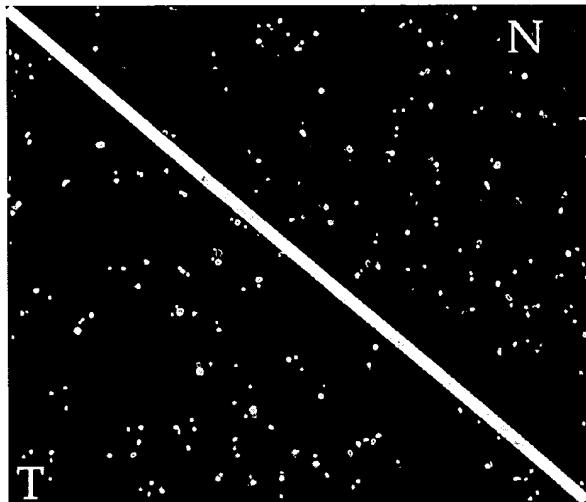
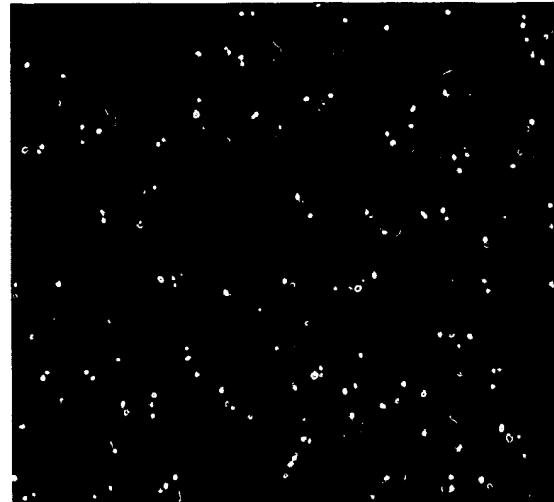
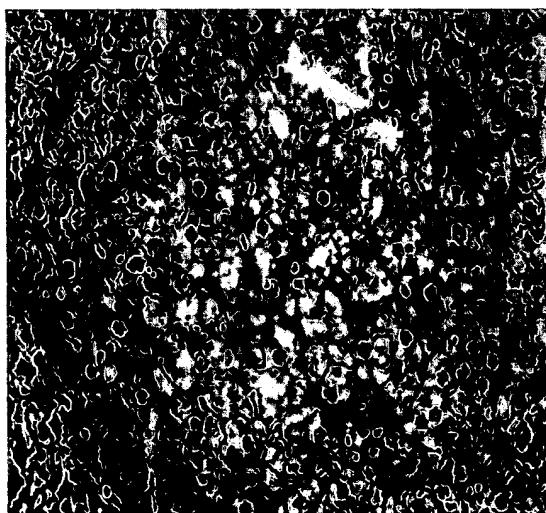


Fig. 7

A

Normal and tumoral tissue

Tumoral tissue
(not metastatic)**B**

Normal tissue

Tumoral tissue
(not metastatic)

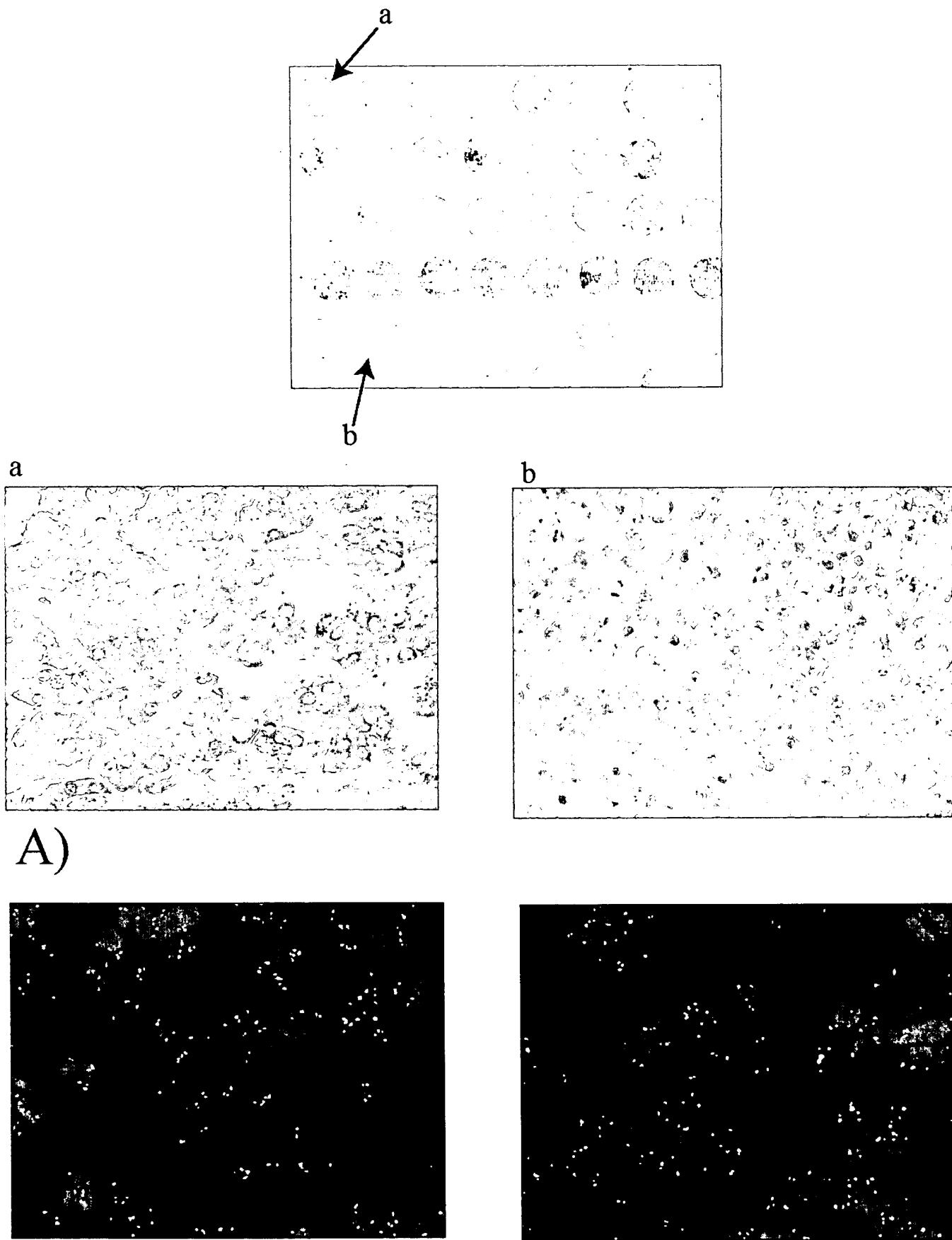
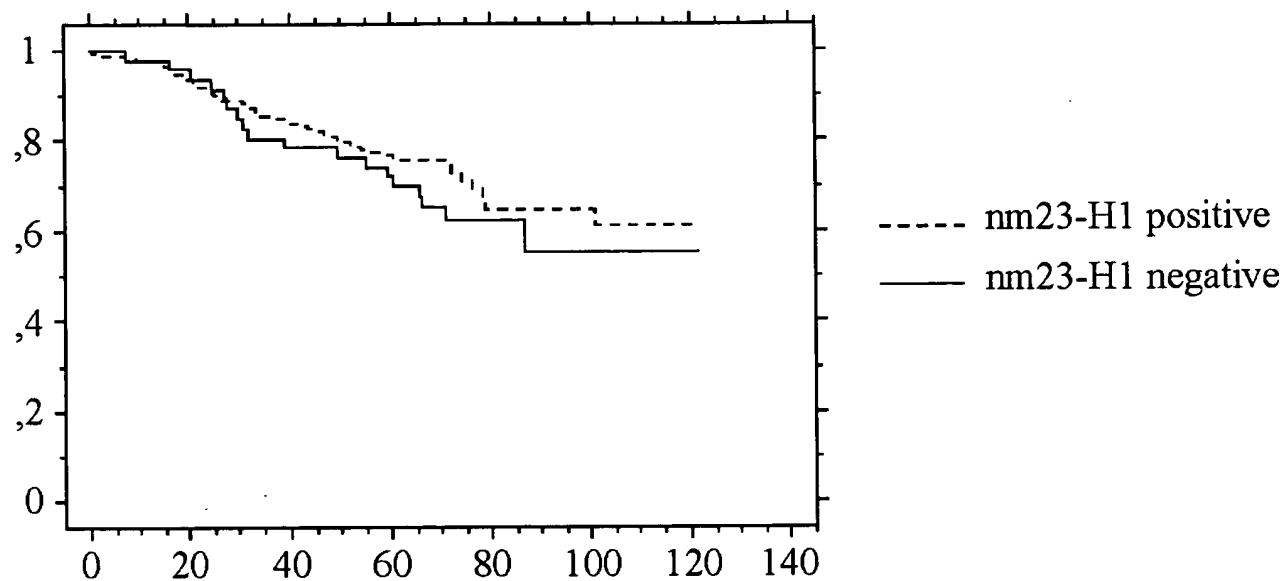


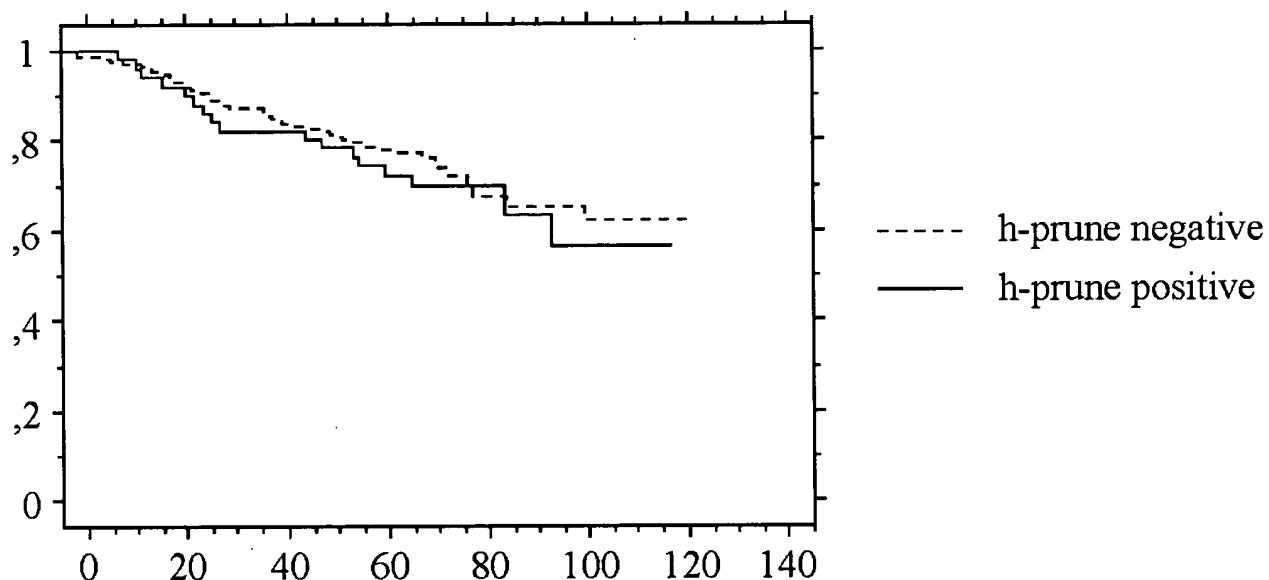
Fig. 9

A)

15/19



B)



C)

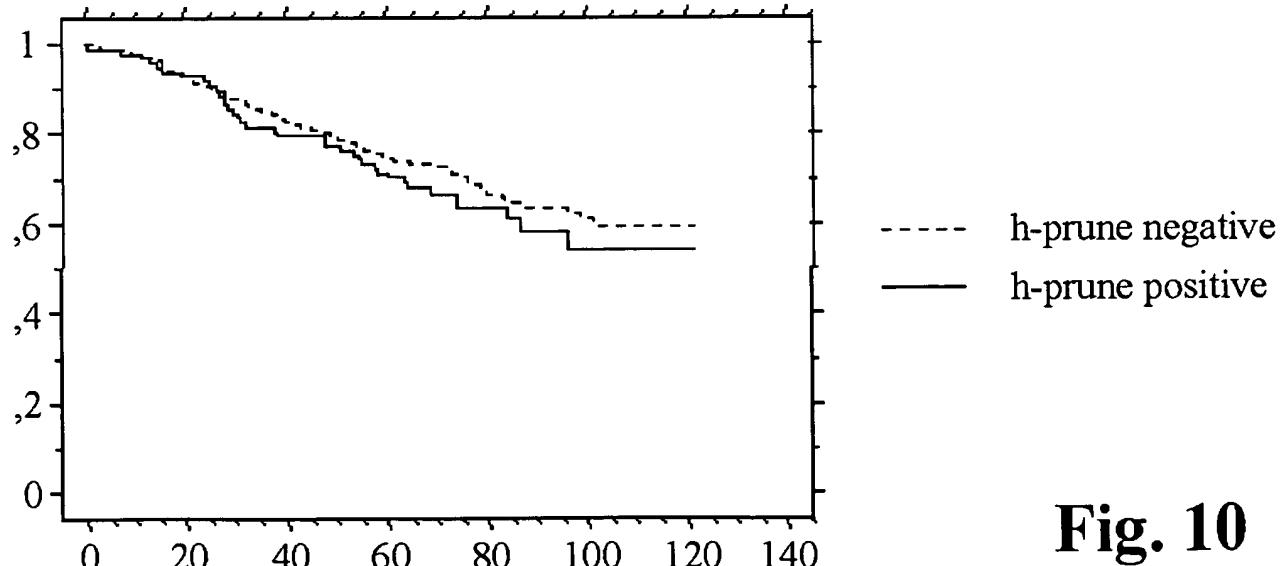
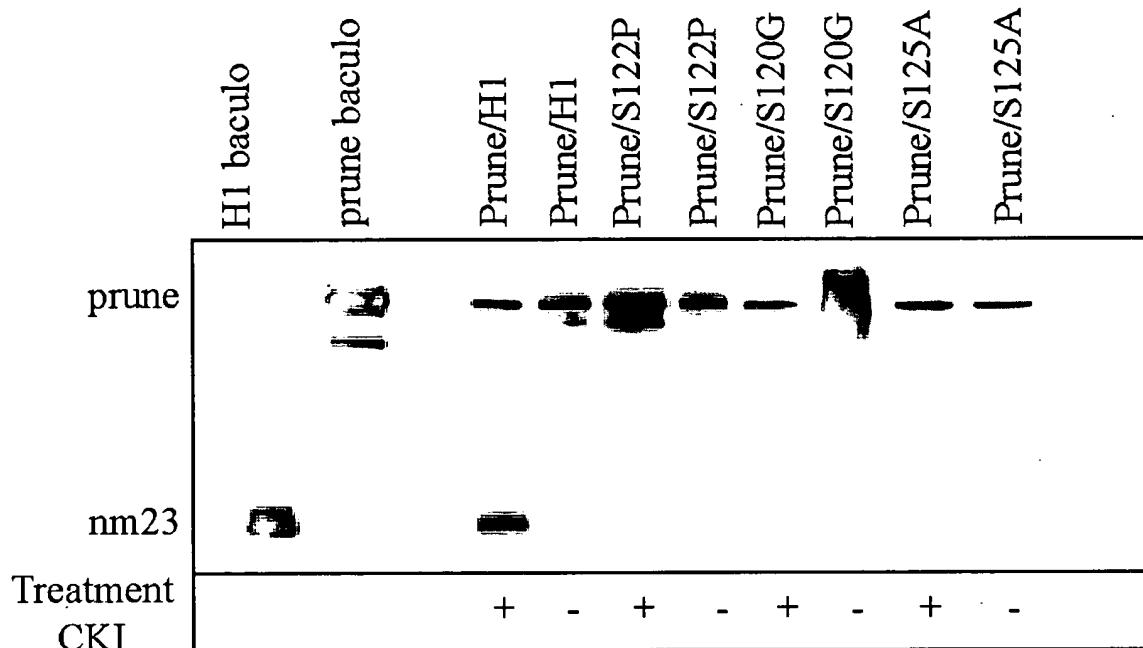


Fig. 10



A)

MYDVPDYASLGSPVEMA
 NLERTFIAIKPDGVQRGLV
 GEIIKRFEQKGFRLVAMK
 FLRASEEHLKQHYIDLKD
 RPFFPGLVKYMNSGPVVA
 MVWEGLNVVKTGRVML
 GETNPADSKPGTIRGDFCI
 QVGRNIIHGSDSVKSAEK
 EISLWFKPEELVDYKSCA
 HDWVYE

B)

Fig. 11

Voyager Spec #1 MC[BP = 1344,6 21449]

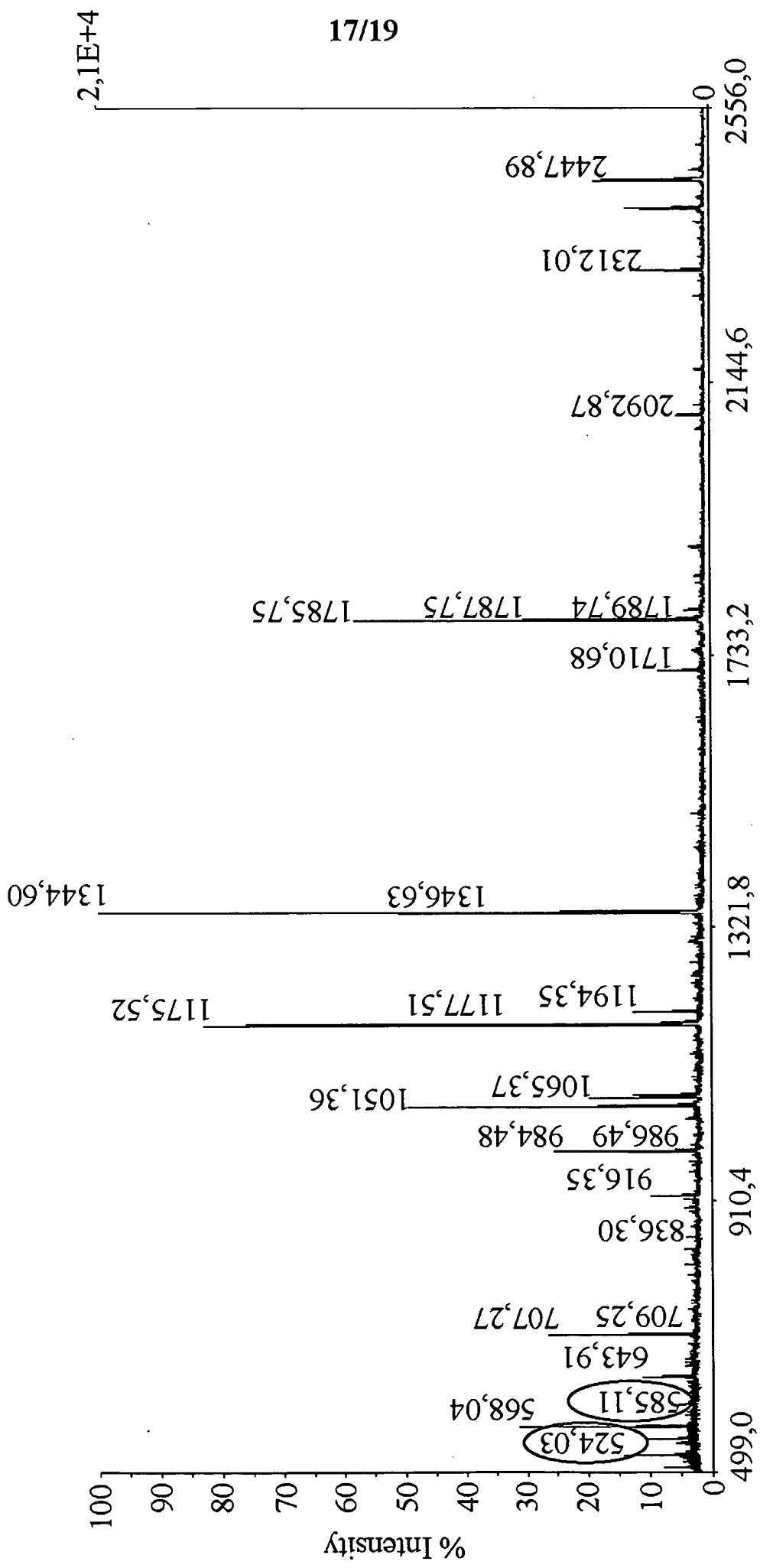


Fig. 11 C

A

	1	2	3	4
CKI δ	+	+	-	-
Isoform Nm23	H1	H2	H1	H2

nm23 → 

B

IC261	0h	2h	4h	6h	8h	0h
CIP	—	—	—	—	—	+
Phosphorecated nmZH1						
Total nm23H1						

C

	1	2	3	4	5
IC261 μMol		50	200	—	

h-prune → 

nm23H1 → 

Fig. 12

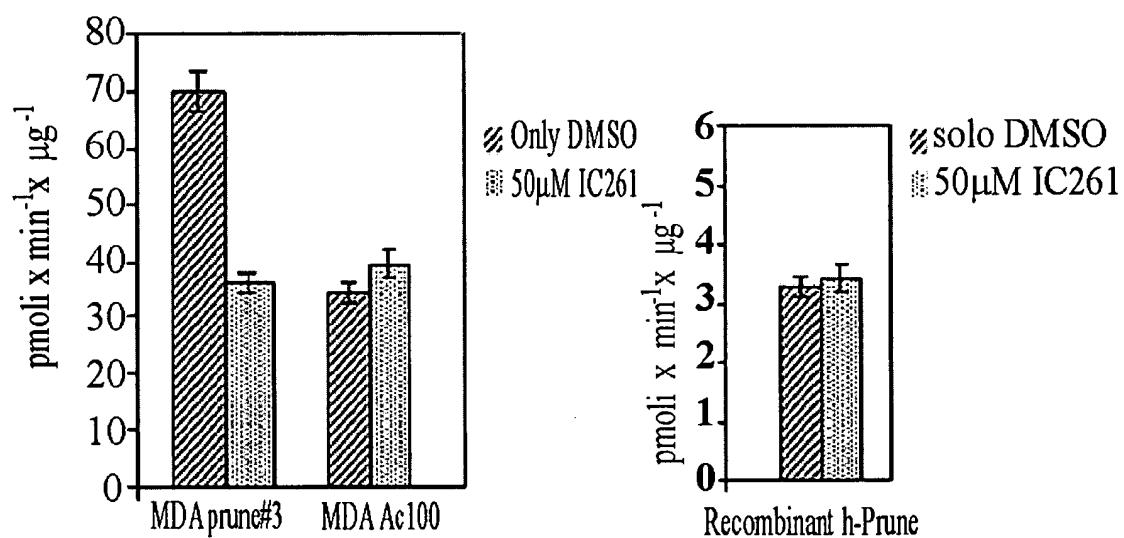
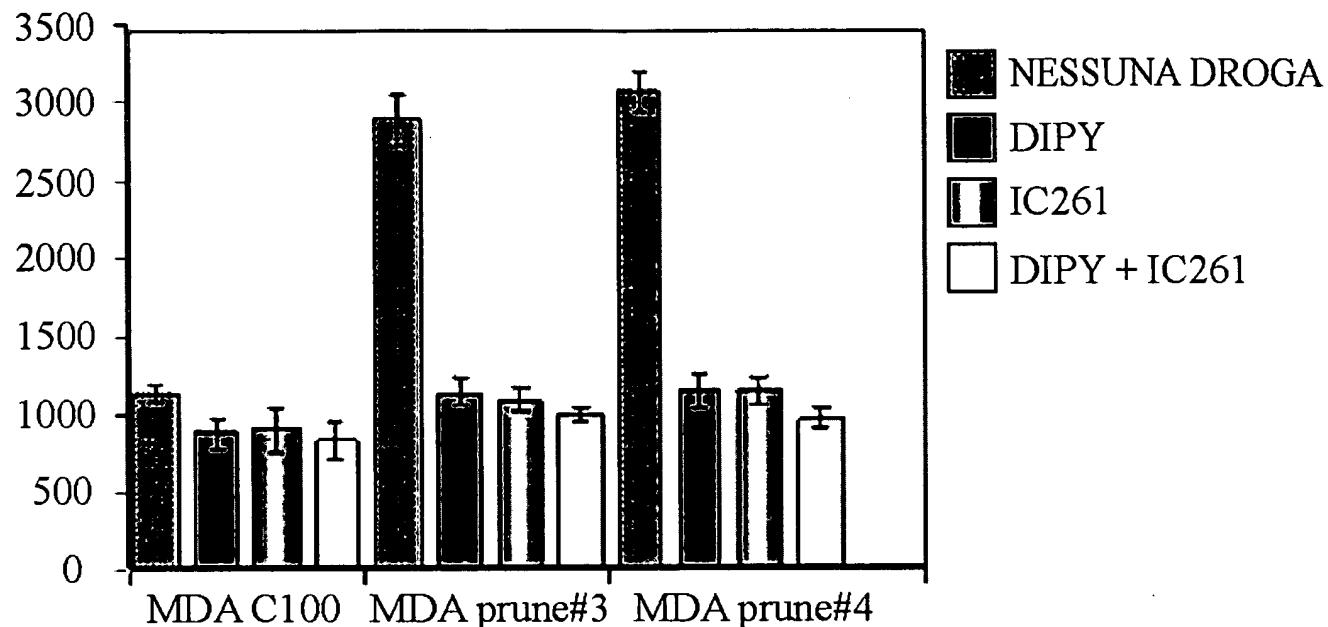


Fig. 13

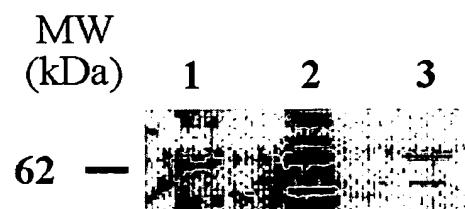


Fig. 14